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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/587,468	11/27/2006	Paolo Morazzoni	2503-1225	5191

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EXAMINER	
MI, QIUWEN	
ART UNIT	PAPER NUMBER
1655	

NOTIFICATION DATE	DELIVERY MODE
12/03/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

DocketingDept@young-thompson.com

Office Action Summary	Application No.	Applicant(s)	
	10/587,468	MORAZZONI ET AL.	
	Examiner	Art Unit	
	QIUWEN MI	1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 October 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23-46* is/are pending in the application.

4a) Of the above claim(s) *43-45* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23-42 and 46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *27 July 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's reply filed on 10/26/09 is acknowledged. Claims 1-22 are cancelled. Claims 23-46 are pending. Claims 43-45 are withdrawn. **Claims 23-42 and 46 are examined on the merits**.

Any rejection that is not reiterated is hereby withdrawn.

Claim Rejections –35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 23-42 and 46 remain rejected under 35 U.S.C. 103(a) as being unpatentable Summers (US 6733797), in view of Loew (Value of Ginkgo biloba in treatment of Alzheimer dementia, Wiener medizinische Wochenschrift (1946), (2002) Vol. 152, No. 15-16, pp. 418-22. Ref: 40), and further in view of Carini et al (Carini et al, Complexation of Ginkgo biloba extract with phosphatidylcholine improves cardioprotective activity and increases the plasma antioxidant capacity in the rat).

This rejection is maintained for reasons of record set forth in the Office Action mailed out on 6/26/2009, repeated below. Applicants' arguments filed have been fully considered but they are not deemed to be persuasive.

Summers teaches the present invention is a supplement combination including at least one, and preferably at least two, phosphoesters and at least one antioxidant (col 3, lines 45-48). The herbal antioxidant comprises at least one member selected from compounds derived from the group consisting of ginkgo biloba etc (col 4, lines 16-32). Summers also teaches a neurochemical formulation comprising a supplement for improving function of neurons, improving memory and cognitive abilities (thus a medicament). Summers teaches a health supplement composition for mammals for improving memory and cognitive abilities comprising: 60 mg ginkgo biloba extract, 22.5 mg phosphatidyl serine (thus 82.5 mg per day), grape pip (proanthocyanidins), manganese, calcium (thus minerals), vitamin B1-B6, vitamins A, C, and E, 675 mg phosphatidyl choline (phospholipid) (col 4, lines 35-40), etc, wherein said use on mammals comprises prevention or treatment of illnesses or conditions selected from the group consisting of a condition requiring memory improvement, cognitive improvement, AIDS-associated dementia, Alzheimer's disease, benign senile forgetfulness, Down's syndrome-associated dementia, Lewy body dementia, multi-infarct dementia, multiple sclerosis, Parkinson's disease-associated dementia, tardive dyskinesia, Wernicke-Korsikoff syndrome, and alcoholism-associated dementia (claim 1; col 8, Table 1). Summers also teaches the composition is administerable via an oral application method (claim 3), and Summers further teach health supplement being ingested as tablets (col 1, lines 25-37). Summers further teach that these certain combinations of substances are found to give improved nervous system function with

improved cognitive function and mental energy (thus treating mental fatigue) (col 6, lines 50-55). At last Summers teach the composition may contain 0 mg to 300 mg phosphatidylserine (col 4, lines 35-40), 0 mg to 16,000 mg of phosphatidylcholine, and 0 mg to 180 mg of ginkgo biloba (col 4, liens 57-63), thus phosphatidylserine, phosphatidylcholine (other phospholipid), and ginkgo biloba extract are result-effective variables for treating Alzheimer's disease.

Summers does not explicitly teach that Ginkgo biloba extracts contains ginkgo flavone glycosides, terpene lactones, a composition comprising acetylcholinesterase, or the claimed amount or ratio of the components, neither does Summers teach the ginkgo complexed with phospholipid.

Loew teaches Ginkgo biloba special extract Egb 761 is a standardized and highly purified extract of Ginkgo leaves. Among the active constituents are the ginkgo-flavone glycosides and the terpene-lactones (ginkgolides, bilobalide). The presence of these constituents in Ginkgo extracts, which constituents are known to be useful for treating Alzheimer's disease, provides the rationale for clinical trials in vascular dementia and primary degenerative dementia of the Alzheimer's disease, and in mixed forms of both. In clinical trials of different working-groups, effects of Ginkgo biloba on the cognitive performance, global function, and activities of the daily living have been found. Metaanalysis in the indication—demential disorders--comparing Ginkgo biloba versus acetylcholinesterase inhibitors have shown a similar clinical efficacy of both therapy regimens with an additional drug safety benefit for Ginkgo. Loew further teaches that clinical trials with fixed combinations of acetylcholinesterase inhibitors with Ginkgo biloba extracts in moderate or severe demantia would be necessary (see Abstract).

Carini et al teach the Ginkgo biloba extract significantly increased the total antioxidant plasma capacity only when complexted with phospholipids (see Abstract). Carini et al also teach "with the native extract (GB (Ginkgo biloba) group) the plasma antioxidant poll tends to increase, although not significantly, which the GB-PC complex significantly increases in respect to the controls both TRAP (total radical trapping antioxidant power) and FRAP (ferric-reducing/antioxidant powder) values, by 24.5 ($p< 0.05$) and 27.9% ($p<0.05$), to indicate a strong enhancement of the antioxidant capacity of plasma, due to an increased enteral absorption of phenolic antioxidants when suitably embedded within a lipophilic carrier (page 329, 2nd column, 2nd paragraph).

It would have been *prima facie* obvious for one of ordinary skill in the art at the time the invention was made to use the composition of Summers in a method of enhancement of cognitive function and reducing mental fatigue, and in the treatment of Alzheimer's disease since the composition yielded beneficial results in improving memory and cognitive abilities, and in the treatment of Alzheimer's disease.

It would have been *prima facie* obvious for one of ordinary skill in the art at the time the invention was made to use the ginkgo-flavone glycosides and the terpene-lactones (ginkgolides, bilobalide from Loew in the treatment of Alzheimer's disease, as Loew explicitly teaches Ginkgo biloba extract contains those components. It would have been *prima facie* obvious for one of ordinary skill in the art to include acetylcholinesterase inhibitors in the composition since Loew teaches Ginkgo biloba has shown a similar clinical efficacy with acetylcholinesterase inhibitors, and clinical trials with fixed combinations of acetylcholinesterase inhibitors with Ginkgo biloba extracts in moderate or severe demantia would be necessary (see Abstract).

It would have been *prima facie* obvious for one of ordinary skill in the art at the time the invention was made to use the complex of Ginkgo biloba and phospholipid from Carini et al since Carini et al teach the complex of Ginkgo biloba and phospholipid strongly increases the antioxidant capacity of plasma. Therefore, it would have been obvious for one of the ordinary skill in the art to use the complex of Ginkgo biloba and phospholipid to enhance the antioxidant capacity of plasma so as to improve function of neurons, improve memory and cognitive abilities of Summers.

Regarding the limitation to the amount of the components, or the ratio of ginkgo and the phosphatidylserine in the composition, the result-effective adjustment in conventional working parameters is deemed merely a matter of judicious selection and routine optimization which is well within the purview of the skilled artisan. It has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. The differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). (Claimed process which was performed at a temperature between 40°C and 80°C and an acid concentration between 25% and 70% was held to be prima facie obvious over a reference process which differed from the claims only in that the reference process was performed at a temperature of 100°C and an acid concentration of 10%.); see also Peterson, 315 F.3d at 1330, 65 USPQ2d at 1382 ("The normal desire of

scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages."); In re Hoeschele, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969) (Claimed elastomeric polyurethanes which fell within the broad scope of the references were held to be unpatentable thereover because, among other reasons, there was no evidence of the criticality of the claimed ranges of molecular weight or molar proportions.). For more recent cases applying this principle, see Merck & Co. Inc. v. Biocraft Laboratories Inc., 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989); In re Kulling, 897 F.2d 1147, 14 USPQ2d 1056 (Fed. Cir. 1990); and In re Geisler, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997). see MPEP § 2144.05 part II A. Although the prior art did not specifically disclose the amounts of each constituent, it would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to determine all operable and optimal concentrations of components because concentrations of the claimed components are art-recognized result effective variables because they have the ability for treating Alzheimer's disease, which would have been routinely determined and optimized in the pharmaceutical art.

From the teachings of the references, it is apparent that one of the ordinary skills in the art would have had a reasonable expectation of success in producing the claimed invention.

Thus, the invention as a whole is *prima facie* obvious over the references, especially in the absence of evidence to the contrary.

Applicant argues that "CARINI fails to teach or suggest the complexation of Gingko with other specific phospholipids other than phosphatidylcholine. Furthermore, CARINI fails to teach or suggest that Gingko complexed with phosphatidylcholine can be used in a possible method for the enhancement of cognitive function and alleviation of mental fatigue" (page 3, 3rd paragraph). Applicant also argues that "CARINI merely mentions, in the Introduction, the possible use of Gingko biloba for treating cerebral ischemia. Even in this limited suggested use of Gingko, CARINI fails to demonstrate any experimental data in this regard. Indeed, CARINI fails to teach or suggest anything that the plasma antioxidant activity of Gingko-phosphatidylcholine complex may be somewhat useful in the brain, or in particular, the enhancement of cognitive function and alleviation of mental fatigue" (page 3, last paragraph bridging page 4). Applicant further argues that "CARINI also fails to teach or suggest to one of ordinary skill in the art any reason to select another phospholipid among the many existing possibilities, and in particular, phosphatidylserine instead of phosphatidylcholine, and then to complex the phospholipid with gingko biloba extract" (page 4, 2nd paragraph). Applicant conclude that "CARINI, like SUMMERS and LOEW, fails to teach or suggest a Ginkgo-phosphatidylserine complex such as that described in the instant specification, and as featured in the instant claims. Specifically, the references fail to recognize that a *Ginkgo biloba* extract complexed with phosphatidylserine has significant effects above a non-complexed Ginkgo extract" (page 4, 3rd paragraph).

This is not found persuasive. First of all, in response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir.

1986). The 103 rejection is based on three references, the main reference Summers teaches a health supplement composition for mammals for improving memory and cognitive abilities comprising: 60 mg ginkgo biloba extract, 22.5 mg phosphatidyl serine (thus 82.5 mg per day). Carini et al teach the Ginkgo biloba extract significantly increased the total antioxidant plasma capacity only when complexted with phospholipids. It would have been *prima facie* obvious for one of ordinary skill in the art at the time the invention was made to use the complex of Ginkgo biloba and phospholipid from Carini et al since Carini et al teach the complex of Ginkgo biloba and phospholipid strongly increases the antioxidant capacity of plasma. Therefore, it would have been obvious for one of the ordinary skill in the art to use the complex of Ginkgo biloba and phospholipid to enhance the antioxidant capacity of plasma so as to improve function of neurons, improve memory and cognitive abilities of Summers.

Applicant argues that "The presently claimed method enhances cognitive function and alleviates mental fatigue, i.e., it improves the factors related therewith such as the speed of memory and memory quality, increases accuracy and attention in activities in normal and healthy subjects, prevents deterioration of the speed and quality of memory in people with decreased cognitive functions, counteracts cognitive fatigue, and influences the mood *(see,* page 4, lines 6-13 of the present application)" (page 4, last paragraph). Applicant also argues that "As indicated at page 6, lines 22-28, and at page 7, lines 1-4 of the present application, Gingko shows a strong affinity for phospholipids, resulting in the generation of bonds which markedly modify the physiochemical and spectroscopic characteristics of the new molecules Therefore, the formation of Gingko phospholipids complexes enables the preparation of new biologically active compositions. In fact, they possess physico-chemical and spectroscopic characteristics which are

markedly different from those of the original components and as such they can be incorporated as active principle into pharmaceutical formulations." (page 5, 1st paragraph). Applicant further argues that "Because the complexation between Gingko and phospholipids modifies the physiochemical and spectroscopic characteristics with respect to the starting (parent) compounds, the different relevant therapeutic activity associated with the different corresponding derived complexes obtainable by complexation of Gingko with the many available different phospholipids was not foreseeable" (page 5, 2nd paragraph). Applicant argues that "As described in the specification, applicants have unexpectedly found that a Gingko biloba extract complexed with phosphatidylserine can be used to enhance cognitive function and alleviate mental fatigue significantly above the levels provided not only by the non-complexed extract but also by the extract complexed with phosphotidylcholine" (page 6, 1st paragraph).

This is not found persuasive. Summers teaches the present invention is a supplement combination including at least one, and preferably at least two, phosphoesters and at least one antioxidant (col 3, lines 45-48). The herbal antioxidant comprises at least one member selected from compounds derived from the group consisting of ginkgo biloba etc (col 4, lines 16-32). Summers also teach that a neurochemical formulation composition for improving memory and cognitive abilities, and reversing free radical damage caused by aging or neurodegenerative disease. Since Carini et al teach the Ginkgo biloba extract significantly increased the total antioxidant plasma capacity only when complexted with phospholipids, one of the ordinary skill in the art would be motivated to use ginkgo complexed with phospholipid to enhance the antioxidant capacity of ginkgo so as to reverse free radical damage caused by aging and enhance cognitive function.

Applicant argues that "One of ordinary skill in the art, in view of the teachings of SUMMER, LOEW and CARINI, would have no reason to select phosphatidylserine, and then to select the 10 to 50% of phosphatidylserine as recited in claim 1, in order to achieve the desired therapeutic purpose - the enhancement of cognitive function and alleviation of mental fatigue" (page 5, last paragraph).

This is not found persuasive. In main reference Summers, Table 2 (col 9) teaches the preferred dosage range of components comprising 0-500 mg Phosphatiday ethanolamine, 0-16 mg Phosphatidyl choline, 0-10,000 mg Phosphatidyl inositol; 0-300 mg Phosphatidyl serine. Thus, when the amount of Phosphatiday ethanolamine is 298 mg, the amount of Phosphatidyl choline is 1 mg, the amount of Phosphatidyl inositol is 1 mg, the amount of Phosphatidyl serine is 300 mg, the percentage of Phosphatidyl serine in phospholipid is 50%. Also, when the amount of Phosphatiday ethanolamine is 298 mg, the amount of Phosphatidyl choline is 1 mg, the amount of Phosphatidyl inositol is 2401 mg, the amount of Phosphatidyl serine is 300 mg, the percentage of Phosphatidyl serine in phospholipid is 10%. Therefore, the claimed 10-50% range overlaps with what Summers teaches.

Applicant's arguments have been fully considered but they are not persuasive, and therefore the rejections in the record are maintained.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Qiuwen Mi whose telephone number is 571-272-5984. The examiner can normally be reached on 8 to 5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Terry McKelvey can be reached on 571-272-0775. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

QM

/Michael V. Meller/

Primary Examiner, Art Unit 1655